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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,653	10/19/2001	Ralph-Heiko Mattern	INT-0004	2405

7590 04/07/2004

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EXAMINER	
NAFF, DAVID M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/002,653	MATTERN ET AL.	
	Examiner	Art Unit	
	David M. Naff	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-9 and 11-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-9 and 11-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment of 1/9/04 canceled claims 1 and 10, and amended claims 2-7, 9 and 13.

Claims examined on the merits are 2-9 and 11-13, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The disclosure is objected to because of the following informalities: at page 8, line 28, the meaning of "USP 24<1211>" and "USP 24<71>" is uncertain. It is uncertain as to the purpose of "<" and ">" and how these symbols relate to the numbers in between and to the number "24". Additionally, it is uncertain as to whether "USP" is an abbreviation or stands for something else.

Appropriate correction is required.

Applicants assert that these are not hyperlinks or patent numbers, but are reference numbers for standardized sterilization protocols and/or validation tests well known to those skilled in the art. However, no publication is apparent reciting the reference numbers as in the specification. If the reference numbers and the protocols and tests they represent are well known as asserted by applicants, copies of publications should be supplied reciting the numbers as in the specification and describing the protocols or tests.

Claim Rejections - 35 USC § 101

Claims 5-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are confusing and unclear by claim 5 requiring a method of producing the scaffold or matrix of claim 13, and not setting forth steps for a complete process to make the scaffold or matrix. In addition to a step of cross-linking the co-precipitate, the method would need steps of producing the co-precipitate.

Claim Rejections - 35 USC § 103

Claims 2-9 and 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yannas et al (4,060,081) or Yannas et al (4,280,954) in view of Li (5,674,290) (newly applied).

The claims are drawn to a scaffold or matrix and method for producing and using the scaffold or matrix wherein the scaffold or matrix comprises a collagen and glycosaminoglycan co-precipitate cross-linked with glutaraldehyde to provide a density of cross-linkages to stabilize the scaffold or matrix toward electron beam radiation at about 15 to about 80 kGy so that the scaffold or matrix retains characteristics to function as a structural support for cell and tissue growth. In some claims, the scaffold or matrix is terminally sterilized with electron beam radiation.

Yannas et al ('081) disclose producing a composition containing a collagen and glycosaminoglycan co-precipitate cross-linked with glutaraldehyde (cols 15 and 16), and which can be sterilized with

irradiation (col 12, line 52). The composition can be used as artificial graft to replace the function of normal skin and provide a template for cellular regeneration (col 14, lines 48-50). A silicone polymer layer may be present (col 13, line 29).

Yannas et al ('954) disclose producing an implant containing a collagen and glycosaminoglycan co-precipitate cross-linked with glutaraldehyde similar to Yannas et al ('081). The cross-linked co-precipitate may be sterilized (col 23, lines 19-37).

Li discloses preparing an implant (col 6, lines 10-24) by co-precipitating collagen and glycosaminoglycan, cross-linking, packaging, and sterilizing with gamma-irradiation (col 6, lines 22-23). Alternative to gamma-irradiation, electron beams may be used for sterilizing (col 6, lines 48-52 and col 1, lines 28-30).

It would have been obvious to use electron bead radiation to carry out irradiation sterilization of the composition of Yannas et al ('081) or the sterilization of Yannas et al ('954) as suggested by Li disclosing electron beam irradiation as an alternative to gamma irradiation for sterilizing an implant made of a cross-linked co-precipitate of collagen and glycosaminoglycan. Li discloses a gamma irradiation dosage of 15 to 35 kGy, and it would have been obvious to employ a similar dosage when using electron beam irradiation. Cross-linking conditions disclosed by Yannas et al ('081) or ('954) will inherently provide a cross-linkage density as claimed to stabilize for electron beam radiation. Moreover, it would have been obvious to provide a cross-linkage density for desired stability since Yannas et

al ('081) disclose that degree of solubility and resistance to resorption can be controlled by the degree of cross-linking (col 9, lines 25-40), and Yannas et al ('954) disclose cross-linking to a desired density (col 8, lines 50-55). The conditions of dependent claims would have been obvious from conditions disclosed by the references. Yannas et al ('081) and ('954) disclose a silicone layer as in claim 2, and Li discloses packaging prior to irradiation as in claim 9. The percent glutaraldehyde in claims 6 and 8 is not unobviously different the concentration of glutaraldehyde used by Yannas et al ('081) and ('954).

Response to Arguments

Applicants urge that Cheung et al uses collagen matrices instead of cross-linked collagen/glycosaminoglycan matrices, and uses gamma radiation instead of electron beam radiation. However, Cheung et al has been replaced with the Li reference, which discloses a cross-linked co-precipitate of collagen and glycosaminoglycan, and the use of electron beam radiation as an alternative to gamma radiation.

Applicants urge that Yannas et al use standard cross-linking with 0.25% glutaraldehyde as in Example 1 of the present specification, and these cross-linking conditions do not stabilize the scaffold or matrix to electron beam radiation at about 15 to about 80 kGy. However, the claims do not require cross-linking conditions sufficiently different from Yannas et al to obtain significantly more stability to electron beam radiation than provided by the cross-linking conditions of Yannas et al. Using a concentration of glutaraldehyde slightly above the

standard amount of 0.25% as in claim 6 would not result in significantly more stability. Further more the tests in the specification used 20 kGy E-beam irradiation. In the claims, the E-beam radiation can be as low as 15 kGy. At this dosage, 0.25% glutaraldehyde may be sufficient for stability. Additionally, Yannas et al ('081) (col 18, lines 1-10) and Yannas et al ('954) (col 15, lines 40-50) use two steps of cross-linking in 0.025 M glutaraldehyde. This would produce the same scaffold or matrix as when using two steps of cross-linking with 0.25% glutaraldehyde as in claim 8, or when using 0.05 M glutaraldehyde as in the specification (page 12, line 3). Longer contact with glutaraldehyde will produce the same density as when using a shorter contact time at a higher concentration of glutaraldehyde.

Claim Rejections - 35 USC § 102

Claims 2-8, 12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Yannas et al (4,060,081) or (4,280,954).

The invention and references are described above.

The cross-linked collagen/glycosaminoglycan matrix of Yannas et al is inherently cross-linked sufficiently to retain characteristics after sterilizing as required by the claims. The matrices of Yannas et al can be sterilized, and it does not appear using electron beam radiation will produce a matrix differing substantially in chemical and physical properties.

Response to Arguments

Applicants urge that results in the specification obtained when using standard conditions as used by Yannas et al as compared with cross-linking conditions of the invention show that Yannas et al do not obtain a matrix having the stability of the claimed scaffold or matrix to electron bean radiation as claimed. However, as set forth above, the claims encompass using the cross-linking conditions of Yannas et al or encompass cross-linking conditions differing so little from those of Yannas et al as not to produce a scaffold or matrix that is materially different. As set forth above, 0.25% glutaraldehyde may provide sufficient stability at 15 kGy, and slightly above 0.25% glutaraldehyde will not produce a significantly different cross-linking density. Furthermore, the two steps of cross-linking at 0.025 M glutaraldehyde of Yannas et al is the same as the two steps of claim 8 using 0.025% glutaraldehyde.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David M. Naff
Primary Examiner
Art Unit 1651

DMN
4/2/04